DERMATOLOGIC RESEARCH: AN OFFICE PROCEDURE?

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This presentation will ask the question can, or how successfully can, dermatologic research be carried out in a regular office practice. Recognizing from the outset that some dermatologic investigation requires hospital and/or laboratory investigation, have not too many dermatologists overlooked or neglected the possibility of carrying out sound and fundamental investigation during their regular office practice?

Our Chairman, Livingood (1), at the annual meeting last year discussed clinical investigation in dermatology and I want to explore the concept that dermatologic research can be carried out in a busy office. Katz (2) has recently given a masterful presentation on medical research and I will quote or paraphrase frequently from his paper. Pillsbury, Zimmermann and Baldridge (3) in 1950 defined necessary controls in clinical dermatologic investigation.

Several capable dermatologists have, I believe, developed the illusion that one must use animals, chemical analyses, complicated mechanical gadgets, culture studies, and the like in order to produce data which are significant. Research is not gadgeteering. Research depends on the pursuit of ideas. One must remember that medical research should be primarily directed toward helping patients and their problems rather than merely to satisfy the curiosity of the investigator. Research should be directed toward finding the truth and not toward proving any given hypothesis. There has been some tendency to consider the good dermatological clinician as a wasted human being unless he produces some so-called fundamental investigation involving the use of animals, laboratory equipment and the like. Good research in dermatology is just as dependent on good diagnosticians and dermatologic therapists as it is on laboratory investigators. A wrong diagnosis of a given patient may negate all the laboratory findings and/or studies performed and, in a like manner, useful and helpful laboratory findings may be worthless without good clinicians to utilize properly available information.

If one but remembers, a well respected laboratory stated that penicillin was worthless in the treatment of syphilis; however, careful clinically controlled evaluation in the human being proved that penicillin was, and is, the best form of therapy available. Before I proceed further, may I point out that this is no attempt to discredit superb investigations well known to us all, that are going on in several dermatologic centers throughout this country, but is to be a plea that more dermatologists participate in the investigative program in our field of medicine. If we are to further dermatology as a real entity it is necessary to have a balanced team. Using baseball as an analogy, a team made up of pitchers, no

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matter how good they may be, would win few ball games. More important than this is that the entire team play together as a unit.

Many practicing dermatologists are too prone to belittle their own observations and to feel that because they are not in a teaching institution, associated with preclinical and clinical divisions, laboratory space, etc., their observations may not be important or fundamental. Research is not necessarily done in a laboratory. It may be conducted in the field, in the office, or by the bedside. The perspective is more important than the location. Time alone may determine whether observations made by a Dr. Smith in a town remote from a teaching institution are or were of real significance.

None of us may be able to duplicate such basic observations as did Sir Thomas Lewis. In his description of the triple response this great physician contributed immeasurably to our knowledge of the physiology of the skin. His equipment was meager; his observations profound. In going through the *Journal of Investigative Dermatology* and *Archives of Dermatology* for the past three years I have made a rough survey of the articles as contained in those journals. Case reports, historical articles and the like are not considered in this survey (Figure 1). Admittedly a personal equation entered into separating one article from another and classifying it as I have done. These articles have been classified roughly as to whether they were, or could have been, done in the office, whether they were carried out in the hospital and/or laboratory, and whether or not they have practical or immediate clinical application. Admittedly those in the less practical group may in time to come be of great clinical and practical value. They have also been separated as to whether they have practical applications for the dermatologic clinician at this time or whether they are purely basic investigations which may have proper application sometime in the future.

From this data you will see that the procedures which were done or could have been done in the office are significantly fewer than those carried out in the hospital and/or laboratories and those with practical application today are fewer than those that may have practical application in the future.

	"Clinical"		"Basic"	
	Office Procedure Possible	Office Procedure Not Feasible	Currently Practical	Not Presently Practical
Journal of Investigative Dermatology				
1953	50%	50%	33%	67%
1954	32%	68%	30%	70%
1955	41%	59%	40%	60%
Archives of Dermatology				
1953	40%	60%	57%	43%
1954	40%	60%	70%	30%
1955	40%	60%	46%	54%

FIG. 1. Research survey

Examples, taken at random, of what may be described as purely clinical investigation are those of Lamb in solar dermatitis, Mahoney using penicillin in the treatment of syphilis, Goeckermann's psoriasis therapy, Hailey and Hailey's description of benign familial chronic pemphigus, Hopkins and Costello's treatment of dermatitis herpetiformis with sulfapyridine, the use of anti-malarials in discoid lupus erythematosus, and the use of calciferol in tuberculosis of the skin.

Examples of investigation in which both clinical observations and associated laboratory studies were combined include the work of Hargraves, Haserick and others in the study of the LE cell phenomenon, Eagle's work on BAL in arsenic and heavy metal reactions, the investigations of Shelley, Sulzberger and Lobitz in the physiology of sweating and the work of Olansky and collaborators in human inoculation syphilis.

More or less purely laboratory investigations include those of Kligman on hair and fungi, Kopf's histochemical studies on alkaline phosphatase, Becker, Fitzpatrick, Montgomery and Lerner's studies on melanogenesis, Hambrick and Blank's whole mounts for the study of the skin and its appendages, Montagna's studies on histology and cytochemistry of human skin and Rothman's study of sebum, to mention only a few.

Which of the above reports represents most important investigation? Can anyone say that the clinical, combined or purely laboratory studies are the most significant or are they mutually synergistic?

May I point out again that this is in no way a condemnation of laboratory research. On the contrary, it is a plea for more research of all types. If dermatology is to survive and progress, more clinical investigations must be encouraged. Dermatological investigation should be judged by scientific and practical merits, its simplicity and originality, rather than to be measured by the size of the grant, the number of animals sacrificed, equipment used, and the bibliography of the investigator. Bigness must not be confused with goodness. A bibliography of fifty papers does not necessarily mean that the author is better than the author who only has three or four papers published. The problem of "negative research" deserves some attention. In the minds of many, research must be positive to be of value. It is gratifying when one can obtain a "yes" answer in a planned study, but a clearcut "no" may be just as useful. So-called negative data may oftentimes be just as important as positive data in the study of a given problem.

Before I am considered a demagogue in these hallowed halls, may I further state that I do not feel for one moment that the mere application of a given fungicide or antibiotic in a series of patients represents the kind of dermatologic investigation for which I make a plea. It is obvious that the clinical application of many new drugs is a necessity and when carefully controlled observations are carried out, with cultural studies before and after their use, proper selection of patients to be treated, valuable information accrues to the dermatologic clinician.

In support of the concept I have attempted to discuss may I present without claim of greatness or of scientific significance the following observations made in imy office during the routine daily practice of dermatology.

Diagnosis	Normal Reaction	White Reaction
Normal Subject	10	0
Atopic Dermatitis	0	18
Dermatographia	1	0
Pemphigus	1	0
Dermatophytosis with Id	2	0
Discoid Lupus Erythematosus	2	0
Scleroderma	2	0
Psoriasis	2	0
Alopecia Totalis or Areata	4	0
Lichen Simplex Chronicus	2	0
Leukemia	1	0
Contact Dermatitis	2	0
Urticaria	4	0
Schamberg's Disease	1	0
Hyperhidrosis	2	0
Erysipelas	1	0
Acute Lupus Erythematosus	2	1
Nummular Eczema	2	1
Neurodermatitis	2	2

FIG. 2. Results of locally applied Trafuril ointment

Trafuril* is a 5% ointment of a nicotinic acid ester (tetrahydrofurfuryl ester of nicotinic acid) which is known to produce an erythematous reaction when rubbed into normal skin. (4) It was noted by Saslaw (5) that in acute rheumatic fever the red reaction did not occur. Many other investigators have evaluated Trafuril in systemic disease and in support of the thesis which I have attempted to present today, it was decided to investigate the reaction of Trafuril ointment locally applied to the skin of patients with varying dermatoses (Figure 2).

From these rather simple observations it was soon obvious that all of the patients with atopic dermatitis developed a white reaction in the area of involved skin. This was not due to stroking the skin, although by and large the ointment was always rubbed in, but the white reaction could be duplicated by the lightest application of the ointment to the involved sites.

Other patients diagnosed as nummular eczema or as "neurodermatitis" also showed a white reaction. These pateints could conceivably have been individuals with atopy. One patient with acute lupus erythematosus showed a white reaction to Trafuril. This patient had an intense erythematous eruption which was generalized and she was under substantial cortisone therapy when tested. There is no immediate explanation for her white reaction, but Dr. Saslaw and others have noted that the lack of erythematous reaction in acute rheumatic fever occurred as a "phase" reaction and perhaps the reaction of this patient is similar.

I had hoped that Trafuril might be used in alopecia areata to produce "stimu-

* The Trafuril ointment used in these studies was supplied through the courtesy of Ciba Pharmaceutical Products, Incorporated, Summit, New Jersey.

lating erythema" and it has been used in this condition but after about a week, the patient's ability to produce erythema declined to where it was negligible. After a few days rest the erythema becomes intense as before and whether or not this is due to the exhaustion of histamine or histamine-like substance should be evaluated further. Admittedly the data in these observations is meager and no claim is made for the importance and significance of these observations. Local application of Trafuril may or may not have usefulness as a diagnostic aid in distinguishing atopy from other ezcemas. Hypothesis as to why the reaction does or does not occur and the mechanism of the "exhaustion" reaction are, to me at least, more than mildly interesting.

My plea again is that more dermatologists, in their office practice daily, consider the influence of climatic conditions, environmental conditions, emotional and tension factors, the effects of liver disease, aging, kidney disease, vascular status, endocrine gland disorders, and the like in the course of many of our ordinary recalcitrant dermatoses. Scientific attainment of the individual is more important than the size of the institution, and the equipment used. As Katz has recently stated, "searchers are more important than researchers."

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